Blepharospasm is defined as involuntary eyelid closure that results in significant visual disability. Usually, blepharospasm is the result of irritating eye diseases, such as corneal ulceration, iritis, or other forms of ocular surface disease. When the ophthalmologic examination fails to reveal a cause of the blepharospasm, then the involuntary closure is described as neurologic blepharospasm (Fig. 8–1). Neurologic blepharospasm can be distinguished from emotional conversion reactions by careful evaluation of the clinical history.\(^1\)\(^,\)\(^2\) Blepharospasm can occasionally be a manifestation of emotional disturbance (conversion reaction), although this etiology is relatively uncommon. When psychiatric disease causes this eyelid disturbance, the condition generally lasts for a period of several days to several months and then resolves. Psychogenic blepharospasm occurs in younger patients with a background history of emotional disturbance. Neurologic blepharospasm represents a form of true dystonia; that is, an involuntary movement disorder thought to be associated with basal ganglia disease. Although there have been questions in the past regarding the cause of neurologic blepharospasm, numerous case histories have accumulated that link benign essential blepharospasm to forms of cranial/cervical dystonia (Meige’s syndrome) (Fig. 8–2).\(^1\)\(^–\)\(^3\) These syndromes may represent the same disease, with essential blepharospasm being an early manifestation of Meige’s syndrome. Patients with benign essential blepharospasm generally present to the ophthalmologists complaining of involuntary eyelid closure, and the evaluation is generally unrevealing for any primary ocular disease. Often, these patients initially are not diagnosed with the condition unless the symptoms remain chronic. Frequent ocular misdiagnoses include dry eye syndrome, ptosis, pseudoptosis, or “nervous habit.” These patients often have other family members with movement disorders, including essential tremor of the hand or head, spasmodic torticollis, spasmodic dysphonia, bruxism, jaw dystonia, or other forms of facial movement disorders.\(^4\)

In many cases, neurologic blepharospasm appears to be a late-onset genetic disorder that may be linked to other movement disorders of the head and neck. Many patients with blepharospasm eventually develop involuntary grimacing and abnormal movements of the head, including head titubations (see Fig. 8–3). Spasmodic torticollis, as well as spasmodic dysphonia and bruxism, eventually may evolve in these patients. The other considerations include inquiring about a past exposure to neuroleptic medications such as haloperidol.
(Haldol). Tardive dyskinesia is a specific condition resulting from exposure to certain neuroleptic medications that can cause severe forms of involuntary blepharospasm. Patients with Parkinson's disease or progressive supranuclear palsy may develop an involuntary form of eyelid closure known as apraxia of eyelid opening. These patients often are unable to open their eyelids, although the degree of spasmodic contractions of the orbicularis muscle is considerably less than that observed with Meige's syndrome or benign essential blepharospasm.

The decision to initiate therapy in these patients depends directly on the degree of disability caused by the involuntary lid movement. Many of these patients will first seek medical attention if they have trouble driving an automobile. Serious automobile accidents resulting from these involuntary eyelid movements have been documented.

The major treatment of this condition involves the use of botulinum A toxin. Early in 1990, the Food and Drug Administration approved this treatment for essential blepharospasm and facial dyskinesia.

If the application of this drug is ineffective, then surgical procedures described in the past may be useful in extended management plans. Alternatively, neuroleptic medications have been tried such as trihexyphenidyl (Artane), clonazepam (Clonopin), and proheptadine (Periactin); however, these medications often are ineffective and can produce serious side effects.

**FIGURE 8–1.** A 65-year-old woman with essential blepharospasm.

**FIGURE 8–2.** Meige's syndrome is defined as essential blepharospasm plus involuntary movements of other muscle groups of the head and neck; involuntary movements of the lower face are common.

**FIGURE 8–3.** Spasmodic torticollis can eventually develop in patients with essential blepharospasm, or Meige's syndrome.
**BOTULINUM A TOXIN**¹,⁵–⁷,¹⁰,¹¹

Botulinum A toxin is a protein with a molecular weight of 150,000 that has a biologic activity dependent on its tertiary structure. Botulinum toxin acts by binding to the presynaptic membrane at the neuromuscular junction, blocking the release of acetylcholine for a period of several months. Striated muscle tissues atrophy in a manner resembling traumatic or surgical denervation. Over a period of several months, collateral axonal sprouting occurs with the regeneration of functioning neuromuscular junctions. The clinical effects are regional, and systemic side effects are rare. To date, no patient has developed systemic botulism intoxication from this therapy.

The drug represents a highly diluted form of botulinum A toxin stabilized with added human serum albumin. The added human serum albumin not only preserves biologic activity but also serves as a marker for the presence of the drug in the vial. The lyophilized material is quantitated by its biologic activity and not from direct measurements of protein quantity. The international unit is equivalent to the LD₅₀ of a white mouse. Because the biologic material can be made with varying biologic activities per nanogram, the absolute measurement of nanograms is not meaningful with respect to the potency of the drug.

The drug is usually injected at 4 to 6 points in the periorbital region (Fig. 8–4). It is important to place the injections in the extreme medial extent of the upper eyelid, close to the lash line, and the extreme lateral extent of the upper eyelid, close to the lash line. A lateral injection is administered over the orbicularis muscle overlying the lateral orbital rim, and another point injection is administered to the lateral lower lid. If substantial involuntary brow movements are present, two injections may be given over the brow (Fig. 8–4). As depicted in Figure 8–4, the multiple injection strategy is clearly superior to alternative strategies for the following reasons:

1. Multiple injections of the drug appear to allow the toxin to form a uniform spread pattern over the innervation of the muscle.
2. The injection formulation tends to minimize complications from unwanted spread of the toxin into deeper orbital structures.

The toxin has to be injected every 3 to 4 months to treat essential blepharospasm and Meige’s syndrome. For hemifacial spasm, the duration of action is distinctly longer, usually 5 to 6 months. Although repeated injections represent an inconvenience to patients, these injections are generally well accepted because the drug appears generally to maintain its efficacy and alternative forms of therapy are less effective.

**FIGURE 8–4.** Usual injection strategy used to treat essential blepharospasm.
Initially, a patient is given a total dose of 20 IU of the toxin on each side and is reevaluated in 2 weeks. If after 2 weeks there is no experienced beneficial effect in the blepharospasm, an additional 20 units is administered to each eyelid. The doses should be individualized from patient to patient. Generally, a total dose between 20 and 100 IU is appropriate for most patients. If a beneficial effect is achieved, then the patient is asked to return in 3 to 4 months for reevaluation of the symptoms and to assess whether further injections should be given. The biologic effects in orbicularis oculi muscle weakening can be assessed after 2 weeks by having the patient forcefully close his or her eyes. Atrophy within the orbicularis oculi muscle has been demonstrated 3 to 4 weeks after injection with the toxin (Fig. 8–5). After a patient has been injected with botulinum toxin, the examine should be able to open the eyelids easily, even if the patient is making maximal effort to close the lids. Failure of the clinician to demonstrate this degree of weakness with forced eyelid closure indicates that the toxin has little to no biologic effect when injected (Fig. 8–6). If the eyelids are substantially weakened and symptoms have not subsided, it is unwise to administer the toxin repeat edly because lagophthalmos and exposure keratopathy may result from further injections.

**FIGURE 8–5 (A and B).** Histologic specimen 5 weeks after injection with botulinum toxin. This specimen demonstrates a large degree of muscle fiber size variability, indicating denervation.

**FIGURE 8–6.** Only the right eye was treated with botulinum toxin. Several weeks after injection, the right eyelid closure is significantly weaker than the left. Weakness accompanies the antispasmodic effects of botulinum toxin.
The toxin actually spreads over a clearly defined area after being injected at a single point. In the past, complications have been regional and have included exposure keratopathy, lagophthalmos from excessive weakening effect of the orbicularis, diplopia from spread of the toxin to the orbit, ptosis from spread of the toxin to the levator palpebrae superioris muscle, and eyelid malpositions from lower lid retractor weakening. Diplopia appears to be related to injections along the medial aspect of the lower lid. It has been postulated and demonstrated by clinical studies that limiting the injection to the lower lid appears to have an effect on the incidence of diplopia. Furthermore, it appears appropriate to avoid the midline of the upper lid and to remain close to the lateral and medial extent of eyelashes when using the upper lid injections. This approach allows for the greatest distance between the injection site and the muscular portion of the levator palpebrae superioris muscle, which lies just posterior to the transverse suspensory ligament of Whitnall in the superior orbit (Fig. 8–7). At doses used to treat blepharospasm, the toxin diffusion is clearly less than 10 to 15 mm, and these injection sites afford the greatest distance between the levator muscle and antagonistic orbicularis oculi. Injecting the upper lid in the lid fold or close to the lid crease results in spread of the toxin into the superior orbit and a higher incidence of ptosis.

Although administration of the toxin has to be repeated over a period of many years to maintain control of these diseases, it does not appear that repeated injections have adverse effects on muscle fibers if the toxin is discontinued (Fig. 8–8). Long-term complications of repeated botulinum toxin injections have yet to be reported. Immunologic resistance has been reported in higher doses used to treat adult-onset spasmodic torticollis and, more recently, blepharospasm.

**FIGURE 8-7.** Ptosis can be a complication of lid injections. This complication resulted from the spread of toxin into the muscular portion of the levator muscle.

**FIGURE 8–8.** Fiber size variability is an indication of denervation. This graph was derived from orbicularis specimens taken from patients with neurologic blepharospasm after repeated injections over several years. The biopsies counted here were from patients who were not treated for 6 months prior to the surgical procedure. Note that there is no difference in fiber size variability or cholinesterase staining pattern compared with controls.
SECONDARY THERAPY

Because many patients with essential blepharospasm will develop Meige’s disease (essential blepharospasm, cranial/cervical movement disorder), consultation with a neurologist may be useful. Occasionally, neuroleptic medications such as clonazepam (Clonopin) and trihexyphenidyl (Artane) can be useful in the treatment of cranial or cervical dystonia. Although blepharospasm and abnormal movements of the head and neck generally do not respond well to neuroleptic medications, these medicines may produce a beneficial effect in approximately 20% of cases.

If botulinum toxin is not effective in treating essential blepharospasm, and the blepharospasm remains debilitating, then a patient should be considered for adjunct surgical procedures.

The following represents a list of adjunct surgical procedures for the treatment of essential blepharospasm and Meige’s syndrome.

Correction of Involutional Ptosis or Eyelid Malpositions

Because involuntary blepharospasm is a chronic, constant symptom, these patients very often undergo accelerated involutional changes in the anatomic structure of their eyelids. Disinsertion of the levator aponeurosis (see Chapter 1, Figs. 1-6, 1-7, and 1-13; Chapter 5, Fig. 5-2) is a very common event in patients with this movement disorder. If a patient has involutional ptosis and presents with blepharospasm, it is preferable to consider correcting the involutional ptosis prior to introducing botulinum toxin therapy. This method affords the maximal possible benefit in botulinum toxin therapy. Failure to correct the ptosis prior to instituting therapy may result in the botulinum toxin worsening the ptotic eyelid position, which could impair the beneficial results of spasm relief from injection of the drug. If there are lid malpositions from excessive horizontal lid laxity or capsulopalpebral fascia dehiscence, then surgical repair should be planned. Lower lid entropion is relatively common in patients with blepharospasm. Irritation from the inverted lower lid lashes can aggravate existing neurologic blepharospasm syndrome by adding a reflex blepharospasm component to the patient’s condition.

Facial Neurectomy

Facial neurectomy (Reynolds’ procedure) has been tried for many years for the treatment of blepharospasm. Because partial facial neurectomy is often followed by nerve regeneration, this procedure has limitations in achieving a sustained beneficial effect. Complete facial neurectomies are disfiguring in areas of the facial muscles that are not involved in the movement disorder. Furthermore, often the blepharospasm is the last movement to be diminished by such radical approaches. Complete facial neurectomy should be reserved for the most severely affected patient, for whom all other methods of medicine and surgery have failed.

Anderson Myectomy and Other Myectomy Procedures

These procedures have become among the most popular for the treatment of blepharospasm. They involve removing the orbicularis oculi muscle as completely as possible while instituting various forms of brow lifts as well as tightening the levator aponeurosis. Because the myectomy procedure involves destroying a substantial portion of the muscle, it may produce irreversible changes in the configurations of the eyelids and face. These procedures should be reserved for the most severely affected patients who are functionally debilitated by the symptoms of this disease and for whom botulinum toxin injections have failed.

Treatment for Hemifacial Spasm

Hemifacial spasm represents a special case of blepharospasm that involves involuntary movements of muscles on one side of the face. These movements are also synchronous in nature, unlike the bilateral blepharospasm. This condition is very stereotyped in its presentation, often occurring as involuntary twitches around the eyelid and advancing to involuntary movement of the lower face. The patients find this condition socially debilitating as well as a constant irritant in interpersonal communications. The condition is thought to be caused
by aberrantly directed blood vessels at the base of the brain, which result in an area of demyelination along the intracranial portion of the 7th nerve. From this area of demyelination, ectopic excitation of the facial nerve and ephaptic transmission of this impulse over the course of the nerve are thought to cause these involuntary contractions of the face.\textsuperscript{21–25}

The past history of therapy has included the use of neurosurgical procedures involving posterior craniotomy with microvascular decompression of the intracranial portions of the 7th nerve. In some cases, this procedure has effectively cured the symptoms of this condition.\textsuperscript{21–23} Because this procedure involves posterior craniotomy, the risk of intracranial surgery has to be weighed against the morbidity caused by the hemifacial spasms. Clearly, most patients find botulinum toxin administration preferable to a posterior craniotomy for the treatment of this condition.

Botulinum toxin dose should be selected with caution as much lower doses are needed in patients with hemifacial spasm. Because this disease represents a form of facial neuropathy with denervation of the facial muscles, the muscles are much more sensitive to lower doses of the toxin. Generally the patient is started with a total dose of 15 units given at four injection points on the side involved. If the patient has lower facial twitching as a prominent component with the blepharospasm, then the zygomatic major and minor muscles are treated with an additional 5 units. If there is a pre-existing dry eye syndrome, even lower total doses should be administered (5 to 10 IU). Clearly, the toxin has been noted to have a longer duration of action with these patients than in those with essential blepharospasm and Meige’s syndrome, and these patients often have to be injected no more than 2 to 3 times per year to maintain the beneficial effects of spasm relief. The toxin injection does need to be repeated on all patients. The patient should be checked 2 to 3 weeks after the injection to ensure that there is no evidence of exposure keratopathy, which is more common in this subgroup of blepharospasm patients.

Long-term management (over 5 to 6 years) of hemifacial spasm with botulinum toxin has been noted to be consistently beneficial.

\textbf{FIGURE 8–9. Typical hemifacial spasm, demonstrating synchronous contractions of muscles supplied by one facial nerve.}
REFERENCES


